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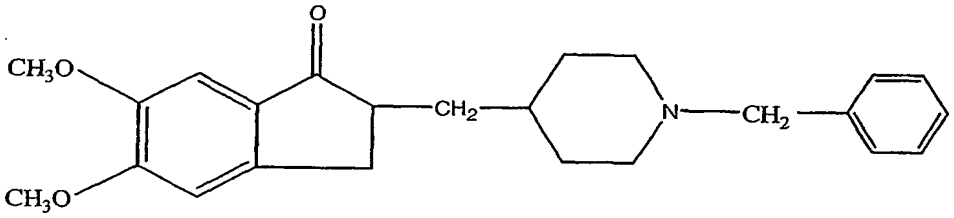
Claims

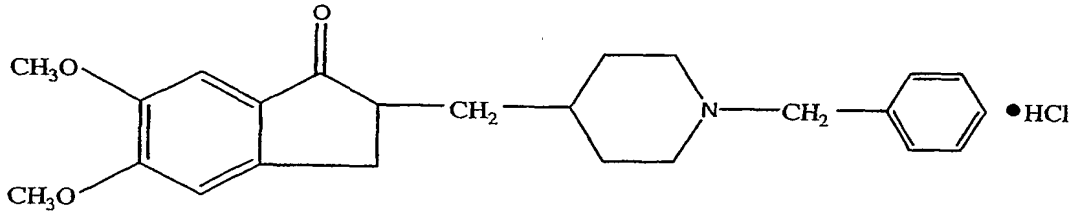
What is claimed is:

1. A method for treating cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy in a patient in need thereof comprising administering a therapeutically effective amount of a compound of formula (IV), a pharmaceutically acceptable salt thereof and/or a stereoisomer thereof:



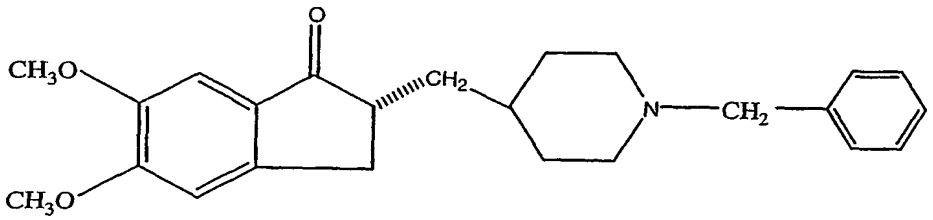
IV.

2. The method of claim 1, comprising administering a therapeutically effective amount of a compound of formula (IVa) or a stereoisomer thereof:



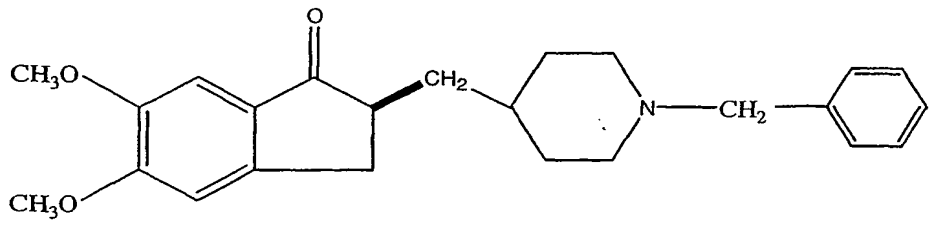
IVa.

3. The method of claim 1, comprising administering a therapeutically effective amount of a compound of formula (VI) or a pharmaceutically acceptable salt thereof:



VI.

4. The method of claim 1, comprising administering a therapeutically effective amount of a compound of formula (VII) or a pharmaceutically acceptable salt thereof:



VII.

5. The method of claim 1, comprising administering to the patient about 1 milligram/day to about 50 milligrams/day of the compound of Formula (IV), the pharmaceutically acceptable salt thereof and/or the stereoisomer thereof.

6. The method of claim 1, comprising administering to the patient about 1 milligram/day to about 25 milligrams/day of the compound of Formula (IV), the pharmaceutically acceptable salt thereof and/or the stereoisomer thereof.

7. The method of claim 1, wherein the compound of Formula (IV), the pharmaceutically acceptable salt thereof and/or the stereoisomer thereof is orally administered to the patient.

8. The method of claim 1, wherein the compound of Formula (IV), the pharmaceutically acceptable salt thereof and/or the stereoisomer thereof is administered to the patient transdermally; by nasal inhalation; or by injection.

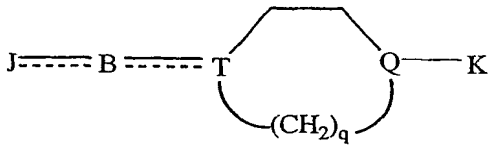
9. The method of claim 1, further comprising administering at least one HMG-CoA reductase inhibitor.

10. The method of claim 9, wherein the HMG-CoA reductase inhibitor is simvastatin, lovastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, or a pharmaceutically acceptable salt thereof.

11. A method for treating cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy in a patient in need thereof comprising administering a therapeutically effective amount of a cholinesterase inhibitor or a pharmaceutically acceptable salt thereof.

12. The method of claim 11, wherein the cholinesterase inhibitor is selected from the group consisting of donepezil, phenserine, tolserine, phenethylnorcymserine, ganstigmine, epastigmine, tacrine, physostigmine, pyridostigmine, neostigmine, rivastigmine, galantamine, citicoline, velnacrine, huperzine, metrifonate, heptastigmine, edrophonium, TAK-147, T-82 and upreazine.

13. The method of claim 12, wherein the cholinesterase inhibitor is a compound of Formula (I), a stereoisomer thereof, and/or a pharmaceutically acceptable salt thereof:



I

wherein J is

(a) a substituted or unsubstituted group selected from the group consisting of (1) phenyl, (2) pyridyl, (3) pyrazyl, (4) quinolyl, (5) cyclohexyl, (6) quinoxalyl, and (7) furyl;

(b) a monovalent or divalent group, in which the phenyl can have one or more substituents selected from (1) indanyl, (2) indanonyl, (3) indenyl, (4) indenonyl, (5) indanedionyl, (6) tetralonyl, (7) benzosuberonyl, (8) indanolyl, and (9) C_6H_5—CO—$CH(CH_3)$—;

(c) a monovalent group derived from a cyclic amide compound;

(d) a lower alkyl group; or

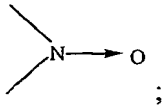
(e) a group of R^{21}—CH=CH—, in which R^{21} is hydrogen or a lower alkoxycarbonyl group;

B is -$(CHR^{22})_r$-, -CO-$(CHR^{22})_r$-, -NR^4-$(CHR^{22})_r$-, -CO-NR^5-$(CHR^{22})_r$-, -CH=CH-$(CHR^{22})_r$-, -OCOO-$(CHR^{22})_r$-, -OOC-NH-$(CHR^{22})_r$-, -NH-CO-$(CHR^{22})_r$-, -CH_2-CO-NH-$(CHR^{22})_r$-, -$(CH_2)_2$-NH-$(CHR^{22})_r$-, -CH(OH)-$(CHR^{22})_r$-, =$(CH-CH=CH)_b$-, =CH-$(CH_2)_c$-, =$(CH-CH)_d$=, -CO-CH=CH-CH_2-, -CO-CH_2-CH(OH)-CH_2-, -$CH(CH_3)$-CO-NH-CH_2-, -CH=CH=CO-NH-$(CH_2)_2$-, -NH-, -O-, -S-, a dialkylaminoalkyl-carbonyl or a lower alkoxycarbonyl;

wherein R^4 is hydrogen, lower alkyl, acyl, lower alkylsulfonyl, phenyl, substituted phenyl, benzyl, or substituted benzyl; R^5 is hydrogen, lower alkyl or phenyl;

r is zero or an integer of about 1 to about 10; R^{22} is hydrogen or methyl so that one alkylene group can have no methyl branch or one or more methyl branches; b is an integer of about 1 to about 3; c is zero or an integer of about 1 to about 9; d is zero or an integer of about 1 to about 5;

T is nitrogen or carbon;

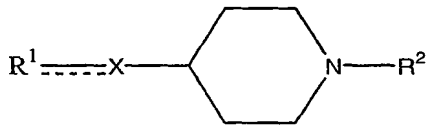
Q is nitrogen, carbon or  ;

q is an integer of about 1 to about 3;

K is hydrogen, phenyl, substituted phenyl, arylalkyl in which the phenyl can have a substituent, cinnamyl, a lower alkyl, pyridylmethyl, cycloalkylalkyl, adamantanemethyl, furylmenthyl, cycloalkyl, lower alkoxycarbonyl or an acyl; and

------ is a single bond or a double bond.

14. The method of claim 12, wherein the cholinesterase inhibitor is a compound of Formula (II), a stereoisomer thereof, and/or a pharmaceutically acceptable salt thereof:



II

wherein R^1 is a (1) substituted or unsubstituted phenyl group; (2) a substituted or unsubstituted pyridyl group; (3) a substituted or unsubstituted pyrazyl group; (4) a substituted or unsubstituted quinolyl group; (5) a substituted or unsubstituted indanyl group; (6) a substituted or unsubstituted cyclohexyl group; (7) a substituted or unsubstituted quinoxalyl group; (8) a substituted or unsubstituted furyl group; (9) a monovalent or divalent group derived from an indanone having a substituted or unsubstituted phenyl ring; (10) a monovalent group derived from a cyclic amide compound; (11) a lower alkyl group; or (12) a group of the formula R^3-CH=C-, where R^3 is a hydrogen atom or a lower alkoxycarbonyl group;

X is $-(CH_2)_n-$, $-C(O)-(CH_2)_n-$, $-N(R^4)-(CH_2)_n-$, $-C(O)-N(R^5)-(CH_2)_n-$, $-CH=CH-(CH_2)_n-$, $-O-C(O)-O-(CH_2)_n-$, $-O-C(O)-NH-(CH_2)_n-$, $-CH=CH-CH=CO-$, $-NH-C(O)-(CH_2)_n-$, $-CH_2-C(O)-NH-(CH_2)_n-$, $-(CH_2)_2-C(O)-NH-(CH_2)_n-$, $-CH(OH)-(CH_2)_n-$, $-C(O)-CH=CH-CH_2-$, $-C(O)-CH_2-CH(OH)-CH_2-$,

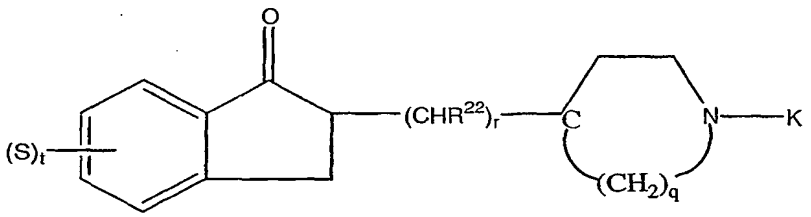
-$CH(CH_3)$-C(O)-NH-CH_2-, -CH=CH-C(O)-NH-$(CH_2)_2$-, a dialkylaminoalkylcarbonyl group, a lower alkoxycarbonyl group;

where n is an integer of 0 to 6; R^4 is a hydrogen atom, a lower alkyl group, an acyl group, a lower alkylsulfonyl group, a substituted or unsubstituted phenyl group, or a substituted or unsubstituted benzyl group; and R^5 is a hydrogen atom a lower alkyl group or a phenyl group;

R^2 is a substituted or unsubstituted phenyl group; a substituted or unsubstituted arylalkyl group; a cinnamyl group; a lower alkyl group; a pyridylmethyl group; a cycloalkylalkyl group; an adamantanemethyl group; or a furoylmethyl group; and

⁻⁻⁻⁻⁻⁻ is a single bond or a double bond.

15. The method of claim 12, wherein the cholinesterase inhibitor is a compound of Formula (III), a stereoisomer thereof, and/or a pharmaceutically acceptable salt thereof:



III

wherein r is an integer of about 1 to about 10; each R^{22} is independently hydrogen or methyl; K is a phenalkyl or a phenalkyl having a substituent on the phenyl ring; each S is independently a hydrogen, a lower alkyl group having 1 to 6 carbon atoms or a lower alkoxy group having 1 to 6 carbon atoms; t is an integer of 1 to 4; q is an integer of about 1 to about 3; with the proviso that $(S)_t$ can be a methylenedioxy group or an ethylenedioxy group joined to two adjacent carbon atoms of the phenyl ring.

16. The method of claim 12, wherein the cholinesterase inhibitor is selected from the group consisting of 1-benzyl-4-((5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine; 1-benzyl-4-((5,6-dimethoxy-1-indanon)-2-ylidenyl)methylpiperidine; 1-benzyl-4-((5-methoxy-1-indanon)-2-yl)methylpiperidine; 1-benzyl-4-((5,6-diethoxy-1-indanon)-2-yl)methylpiperidine; 1-benzyl-4-((5,6-methnylenedioxy-1-indanon)-2-yl)methylpiperidine; 1-(m-nitrobenzyl)-4-((5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine; 1-cyclohexylmethyl-4-((5,6-dimethoxy-

1-indanon)-2-yl)methylpiperidine; 1-(m-fluorobenzyl)-4-((5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine; 1-benzyl-4-((5,6-dimethoxy-1-indanon)-2-yl)propylpiperidine; 1-benzyl-4-((5-isopropoxy-6-methoxy-1-indanon)-2-yl)methylpiperidine; and 1-benzyl-4-((5,6-dimethoxy-1-oxoindanon)-2-yl)propenylpiperidine; a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof.

17. The method of claim 12, comprising administering to the patient about 1 milligram/day to about 50 milligrams/day of the cholinesterase.

18. The method of claim 12, wherein the cholinesterase inhibitor is administered orally, transdermally, by nasal inhalation or by injection.

19. A pharmaceutical composition comprising at least one cholinesterase inhibitor, at least one HMG-CoA reductase inhibitor, and a pharmaceutically acceptable carrier.

20. The pharmaceutical composition of claim 19, wherein the cholinesterase inhibitor is donepezil; and the HMG-CoA reductase inhibitor is simvastatin, lovastatin, pravastatin, fluvastatin, atorvastatin, or cerivastatin.

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